Journal of Exposure Analysis and Environmental Epidemiology (2005), 47–50

www.nature.com/jea

Dermal exposure assessment to benzene and toluene using charcoal cloth pads

BERNA VAN WENDEL DE JOODE,[a,b] ERIK TIELEMANS,[a] ROEL VERMEULEN,[c] HILLION WEGH,[d] AND HANS KROMHOUT[b]

[a]*Department of Chemical Exposure Assessment, TNO Chemistry, Zeist, The Netherlands*
[b]*Environmental and Occupational Health Division, Institute for Risk Assessment Sciences (IRAS), Utrecht University, Utrecht, The Netherlands*
[c]*Occupational and Environmental Epidemiology Branch, Division of Cancer Epidemiology and Genetics, National Cancer Institute, Rockville, USA*
[d]*Environmental Technology, Wageningen University and Research Center, Wageningen, The Netherlands*

Charcoal cloth pads have been used to assess volatile chemicals on the skin in a laboratory setting; however, they have not yet been applied to measure dermal exposure in occupational settings. This study aimed at evaluating whether charcoal pads can be used to assess dermal exposure to benzene and toluene in workers of a petrochemical plant. Inhalation and dermal exposure levels to benzene and toluene were assessed for workers of a petrochemical plant performing different jobs. Benzene uptake was assessed by determining *S*-phenylmercapturic acid in workers' urine samples. Dermal exposure levels on the charcoal pads were adjusted for ambient air levels of benzene and toluene by subtracting the amount of benzene or toluene measured in personal air from the amount of benzene or toluene measured on the charcoal pad. In general, measured external and internal exposure levels were low. The estimated contribution of the dermal route to internal benzene exposure levels was less than 0.06% for all jobs. Toluene personal air concentrations and benzene and toluene dermal exposure levels differed statistically significantly between job titles. For benzene, differences between jobs were larger for adjusted dermal exposures (maximum 17-fold, $P = 0.02$) than for inhalation exposures (maximum two-fold, $P = 0.08$). Also for toluene, although less clear, differences between jobs were larger for adjusted dermal exposures (maximum 23-fold, $P = 0.01$) as compared to inhalation exposures (maximum 10-fold, $P = 0.01$). Charcoal pads appeared to measure dermal exposures to benzene and toluene in addition to ambient air levels. Future studies applying charcoal cloth pads for the dermal exposure assessment at workplaces with higher dermal exposure to organic solvents may provide more insight into the biological relevance of dermal exposure levels measured by charcoal cloth pads. In addition, the design of the dermal sampler might be improved by configuring a dermal sampler, where part of the sampler is protected against direct contact and splashes, but still permeable for the gas phase. This design would most likely result in a better ability to correct for airborne concentrations at a given body location.
Journal of Exposure Analysis and Environmental Epidemiology (2005) **15,** 47–50. doi:10.1038/sj.jea.7500349
Published online 14 April 2004

Keywords: *dermal exposure, charcoal cloth pads, benzene, toluene.*

Introduction

Cohen and Popendorf reported in 1989 on the use of absorptive pads of charcoal cloth to assess volatile chemicals on the skin based on laboratory test results (Cohen and Popendorf, 1989). They concluded that the charcoal cloth dosimeters could be used to assess dermal exposure to volatile chemicals with reasonable accuracy and precision. However, as far as we know, no studies to date have actually applied this method to measure dermal exposure in occupational settings. Consequently, its applicability in field situations remains unknown. However, dermal exposure assessment to organic solvents may provide useful information that cannot be obtained by biological monitoring only, especially when evaluating control measures, glove breakthrough, or pathways of exposures.

A potential limitation in the applicability of charcoal cloth pads is that they do not only measure dermal exposure to droplets and aerosols but also absorb organic vapors through passive diffusion, potentially necessitating a correction for ambient levels of the organic compounds.

The aim of this study was to evaluate whether charcoal pads can be used to assess dermal exposure to benzene and toluene in workers of a petrochemical plant.

Methods

Full-shift personal inhalation exposure levels (passive organic vapor monitors (OVM), 3M^{tm} 3500) and dermal exposure levels were assessed for 35 workers of a petrochemical plant performing activities related to shutting down the plant, maintenance, and starting up the plant. Seven of the 35 workers were measured on two occasions. Activated charcoal

1. Address all correspondence to: B. Van Wendel de Joode, Environmental and Occupational Health Division, Institute for Risk Assessment Sciences (IRAS), Utrecht University, PO Box 80176, 3508 TD Utrecht, The Netherlands. Tel.: +31 30-253-9449. Fax: +31-30-253-9499.
E-mail: b.vanwendel@iras.uu.nl
Received 24 July 2003; accepted 19 December 2003; published online 14 April 2004

cloth pads (Carbopad^{tm}), composed of a layer of charcoal cloth pouched between a layer of cotton and nonwoven cloth, of $4 \times 3\,cm^2$ were worn on the wrist of the hand of preference to assess dermal exposure. In addition, 27 subjects provided a postshift urine sample, and six subjects at two occasions. All samples were stored at $-20^{\circ}C$. Prior to analysis a $\varnothing$ 30 mm segment ($\pm 60\%$ of total pad surface) was punched out of each charcoal pad. Subsequently, benzene and toluene concentrations of the OVM and dermal samples were determined by gas chromatography (GC-FID) according to NIOSH method 1501 (NIOSH, 1994). Limits of detection (LOD) were 0.16 and $0.07\,mg/m^3$ for inhalation exposures *versus* 0.15 and $0.16\,\mu g/cm^2$ for dermal exposures for, respectively, benzene and toluene. Samples below the limit of detection were set on two-third of the corresponding LOD.

Recoveries of charcoal pads for both toluene and benzene ranged from 85% to 100% (average recovery was 95% for both benzene and toluene) as determined in triplicate over a range of benzene and toluene concentrations ($n = 14$; 0.9–90 μg pad ($\varnothing$ 30 mm)).

In order to compare the absorption efficiency of organic vapors by charcoal cloth pads with passive OVM, a laboratory experiment was performed, simultaneously exposing charcoal cloth pads and OVM ($n = 22$) to six different air concentrations ranging from 48.6 to $1630\,mg/m^3$ of benzene and 48.2 to $1610\,mg/m^3$ of toluene, during 120 ($n = 6$), 180 ($n = 6$), 240 ($n = 6$), and 255 ($n = 4$) min. Charcoal pads and OVM appeared to absorb comparable amounts (μg) of benzene and toluene; the efficiency of charcoal pads as compared to OVM was 0.97 (standard deviation (SD) 0.34) and 1.04 (SD 0.34), for benzene and toluene, respectively. The absorption efficiency of charcoal pads was not influenced by concentration or by duration of exposure (data not shown).

As the laboratory experiments indicated that OVM and charcoal pads have comparable absorption efficiencies for benzene and toluene vapors, personal dermal exposure levels were adjusted for benzene and toluene air concentrations by subtracting the amount of benzene or toluene (μg) measured on the corresponding OVM from the amount of benzene or toluene (μg) measured on the charcoal pad. Adjusted dermal exposure values at or below 0 (benzene, $n = 15$; toluene, $n = 9$) were set at two-third of the smallest positive adjusted dermal exposure value (for benzene $= 0.07\,\mu g$; toluene $= 0.05\,\mu g$).

In order to estimate benzene uptake, *S*-phenylmercapturic acid (SPMA), a urinary benzene metabolite, was measured according to a method described by Van Sittert et al. (1993). The LOD was 10 nmol SPMA/l urine. Samples below the limit of detection were set on two-third of the corresponding LOD. All statistical analyses were performed on log-transformed values as exposures and urinary metabolite concentrations followed essentially a log-normal distribution.

Mixed linear regression models (PROC MIXED, method of restricted maximum likelihood (REML)) were applied to estimate the effect of "job", included as a *fixed effect* on inhalation and dermal exposure levels and urinary SPMA levels. For each job, geometric means (GMs) were predicted by taking the exponent of the sum of the least-squares mean group estimates and the true underlying mean of log-transformed exposure averaged over all strata derived from the described mixed-model ($GM = \exp^{(\mu+\beta)}$). In these models, "worker" was included as a *random effect*. In order to explore associations of internal exposure levels (nmol SPMA/l urine) with inhalation and adjusted dermal exposures to benzene, Pearson's correlation coefficients were estimated for logged values. All statistical analyses where performed with SAS System Software V8.2^{TM}.

Relative contributions of the inhalable and dermal pathway to internal benzene exposure were calculated for each job on the basis of the predicted exposure levels, by assuming an inhaled volume of $10\,m^3$ during a working day with 50% of inhaled benzene being absorbed (Yu and Weisel, 1998) and an exposed skin surface of $1000\,cm^2$ (e.g., hands) with a minimal uptake of 0.05% and a maximal uptake of 0.1% (EPA, 2002).

Results

For inhalation exposures, six (14%) and eight (19%) out of 42 samples were below the limit of detection for benzene and toluene, respectively. With regard to unadjusted dermal exposures, all samples showed detectable amounts of benzene and only three (7%) out of 42 samples had undetectable amount of toluene. Two (6%) out of 33 urine samples were below the limit of detection.

Log-transformed inhalation and unadjusted dermal exposure levels for benzene and toluene (mg/m^3) were moderately to strongly correlated: Pearson's $r = 0.65$ ($P < 0.0001$) and $r = 0.86$ ($P < 0.0001$), respectively. Log-transformed inhalation and adjusted dermal exposure levels were still correlated, however, to a lesser extent as observed for the unadjusted dermal exposure levels: Pearson's $r = 0.48$ ($P < 0.01$) and $r = 0.67$ ($P < 0.001$) for benzene and toluene, respectively.

Table 1 shows predicted GMs of inhalation, unadjusted and adjusted dermal exposure levels to benzene and toluene, and urinary SPMA levels. Inhalation exposures to benzene were slightly higher for operators and mechanics performing pitching activities (pitching consists of the placement of partition components into the plant's pipes) than for mechanics performing miscellaneous activities, and cleaners and safety personnel. Pitching mechanics had the highest adjusted dermal benzene exposure levels. Their levels were slightly higher than for operators and considerably higher than for individuals performing other jobs (GMs differed by

Table 1. Predicted GMs with 95% confidence intervals (CI) of inhalation (mg/m^3), unadjusted and adjusted dermal (μg/cm^2 8 h) exposure levels of benzene and toluene, and urinary SPMA levels (nmol SPMA/l urine).

			Inhalation exposure (mg/m^3)		Unadjusted dermal exposure (μg/cm^2 8 h)		Adjusted dermal exposure (μg/cm^2 8 h)				Urinary SPMA levels (nmol SPMA /l urine)
Job	N^a	K^b	Benzene	Toluene	Benzene	Toluene	Benzene	Toluene	N^a	K^b	
Operators	13	11	0.39 (0.24–0.62)	1.12 (0.40–3.17)	2.37 (1.05–5.36)	11.99 (3.78–38.09)	0.74 (0.15–3.65)	4.93 (0.88–27.57)	12	11	31 (21–46)
Mechanics pitching	9	9	0.33 (0.19–0.57)	0.53 (0.15–1.85)	2.96 (1.11–7.89)	2.88 (0.74–11.27)	1.01 (0.17–6.11)	1.19 (0.16–8.94)	4	4	22 (11–43)
Mechanics miscellaneous	7	6	0.24 (0.13–0.44)	0.11 (0.03–0.46)	0.80 (0.27–2.44)	0.69 (0.15–3.25)	0.15 (0.02–1.14)	0.31 (0.03–3.01)	7	6	18 (11–31)
Cleaners, safety personnel	13	9	0.21 (0.13–0.35)	0.27 (0.10–0.77)	0.46 (0.20–1.04)	0.89 (0.28–2.86)	0.06 (0.01–0.29)	0.21 (0.04–1.23)	10	6	23 (15–35)
Total	42	35	0.29 (0.22–0.38)	0.38 (0.22–0.66)	1.27 (0.75–2.16)	2.42 (1.17–5.00)	0.29 (0.11–0.74)	0.87 (0.32–2.38)	33	27	24 (19–31)

[a]Total number of measurements.
[b]Number of subjects.

a factor of 7 and 17). For unadjusted dermal benzene exposures, the differences between jobs were smaller: a factor of 4 and 6, respectively. Calculations of the relative contribution of the dermal route to internal benzene exposure levels showed that for all jobs the dermal contribution was minimal ($\leq 0.06\%$).

Inhalation exposure to toluene was highest for operators, a factor of 10 higher than for mechanics performing miscellaneous activities. For toluene, operators had the highest adjusted dermal exposure levels; their GM was a factor 23 higher than GM for cleaners and safety personnel, whereas unadjusted dermal exposure levels were a factor 13 higher.

GMs of internal exposures were similar for the different jobs ranging from 18 nmol SPMA/l urine for mechanics performing miscellaneous activities, to 31 nmol SPMA/l urine for operators. Log-transformed inhalation levels for benzene showed a weak, statistically significant, association with log-transformed urinary SPMA levels ($r = 0.38$, $P = 0.02$), while for log-transformed adjusted dermal exposures no such association was found ($r = 0.06$, $P = 0.74$). Creatinine-adjusted SPMA levels were somewhat less associated with benzene inhalation levels than unadjusted SPMA levels, and were not associated with adjusted dermal exposures. Controlling for smoking did not alter the results. The correlation coefficients for dermal-urine and inhalation-urine were similar when nonparametric correlation analyses (Spearman) were performed.

Discussion and conclusion

In general, measured inhalation exposure levels were well below the Dutch 8-h time-weighted average occupational exposure limit of 3.25 and 150 mg/m^3 for benzene and toluene, respectively. Urinary SPMA concentrations were overall low, just above the limit of detection.

Toluene personal air concentrations, and benzene and toluene dermal exposure levels differed statistically significantly between job titles. For benzene, differences between jobs were larger for adjusted dermal exposures (maximum 17-fold, $P = 0.02$) than for inhalation exposures (maximum two-fold, $P = 0.08$). Also for toluene, although less clear, differences between jobs were larger for adjusted dermal exposures (maximum 23-fold, $P = 0.01$) as compared to inhalation exposures (maximum 10-fold, $P = 0.01$).

Charcoal pads appeared to be able to measure dermal exposure in addition to the vapor phase, possibly caused by exposure to small droplets or contact with contaminated surfaces. Although more volatile, benzene showed a weaker association between dermal and inhalation exposure than toluene, indicating that possibly the underlying exposure processes differ. To be able to interpret concentrations measured on charcoal pads, inhalation exposure must be monitored simultaneously, because charcoal pads absorb gaseous solvents at the same time. However, adjusting dermal exposure for inhalation exposure levels has limitations. The air concentration measured at chest height might be lower than the air concentration at wrist level due to its increased proximity to the actual source, resulting in an underestimation of the contribution of gaseous solvents to measured dermal exposures. On the other hand, gloves and sleeves might partly have covered the charcoal pads, reducing airborne concentrations at the wrist. In addition, as the charcoal cloth acts like a perfect sink, the derived exposure estimate should be regarded as the upper limit of dermal exposure as evaporation from the skin to the atmosphere is

not taken into account. This later process can be substantial for volatile compounds (Roy et al., 1996).

The biological relevance of dermal exposures measured by charcoal pads remains unclear, as this study did not show an association between dermal exposure levels and internal exposure values, whereas for air concentrations a weak correlation was found with internal exposure values. The only weak correlation for inhalation exposures and the absence of a correlation for dermal exposure levels is most likely due to the relatively low exposure levels measured. Hence, the estimated contribution of the dermal route to internal benzene exposure, levels was less than 0.06% for all jobs. Although SPMA is thought to be one of the most sensitive markers for benzene exposure it is only able to reliably detect inhalation exposure levels down to 1 mg/m^3 (8-h time-weighted average) (Boogaard and van Sittert, 1995).

Future studies applying charcoal cloth pads for dermal exposure assessment at workplaces with higher dermal exposure to organic solvents may provide more insight in the biological relevance of dermal exposure levels measured by charcoal cloth pads. In addition, the design of the dermal sampler might be improved by configuring a dermal sampler, where part of the sampler is protected against direct contact and splashes but still permeable for the gas phase. This design would most likely result in a better ability to correct for airborne concentrations at a given body location.

Acknowledgements

We are grateful to the workers for participating in this study.

References

Boogaard P.J., and van Sittert N.J. Biological monitoring of exposure to benzene: a comparison between S-phenylmercapturic acid, *trans, trans*-muconic acid, and phenol. *Occup Environ Med* 1995: 52(9): 611–620.

Cohen B.S., and Popendorf W. A method for monitoring dermal exposure to volatile chemicals. *Am Ind Hyg Assoc J* 1989: 50(4): 216–223.

EPA. *Toxicological Review of Benzene (Noncancer Effects)*. Integrated Risk Information System (IRIS), US Environmental Protection Agency, Washington, DC, 2002.

NIOSH. Hydrocarbon Aromatics: Method 1501. http://www.cdc.gov/niosh/nmam/nmammenu.html *NIOSH Manual of Analytical Methods (NMAM®)*, 4th edn National Insitute of Occupational Safety and Health, 1994.

Roy A., Weisel C.P., Lioy P.J., and Georgopoulos P.G. A distributed parameter physiologically-based pharmacokinetic model for dermal and inhalation exposure to volatile organic compounds. *Risk Anal* 1996: 16(2): 147–160.

Van Sittert N.J., Boogaard P.J., and Beulink G.D. Application of the urinary *S*-phenylmercapturic acid test as a biomarker for low levels of exposure to benzene in industry. *Br J Ind Med* 1993: 50(5): 460–469.

Yu R., and Weisel C.P. Measurement of benzene in human breath associated with an environmental exposure. *J Expos Anal Environ Epidemiol* 1998: 6: 261–277.